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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/579,738	05/26/2000	Daniel A. Vallera	11983-004001	1069

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/579,738	Applicant(s) VALLERA ET AL.	
	Examiner Q. Janice Li	Art Unit 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11/7/02 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): *See Continuation Sheet*.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-34 and 36-43*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

Continuation of 3. Applicant's reply has overcome the following rejection(s): Applicant's reply has overcome the following rejection(s): Sequence compliance requirement and Written Description rejection and a portion of the enablement rejection closely related to the Written Description rejection under 35 USC 112, 1st paragraph.

Continuation of 5. does NOT place the application in condition for allowance because: It is noted that even though the amended claims drawn to target cells and method of making such are clearly drawn to ex vivo, claim 34 is directed to administration of an ex vivo transfected T lymphocytes to a subject for treatment of any disease in vivo, thus, the claims would be evaluated by the standard. The arguments to enablement rejection under 35 USC 112, 1st paragraph, are not persuasive because the specification fails to provide sufficient guidance for treating any pathogenic cell disease, and the citations of clinical success in treating a wide variety of pathogenic cell diseases with immunotoxic molecules per se could not be used as the support for the instant invention because the success of the cited art in disease treatment was not achieved by using transfected T lymphocytes. Applicants assume in the arguments "provided a sufficiently high amount of immunotoxic molecules is delivered to relevant pathogenic cells, the immunotoxic molecules can be effective in treating the appropriate pathogenic cell disease". One of the critical elements for enabling the claimed invention is how to provide a sufficiently high amount of immunotoxic molecule to pathogenic cells for a sustained period of time. The pharmacokinetics, biodistribution, and mode of operation of a toxic molecule are distinct from a vector-transfected T lymphocytes, how such cells function in vivo and be delivered in a sufficiently high amount to any pathogenic cell anywhere in the body of a subject so that a therapeutic effect could be achieved could not be predictably extropolated from the transient inhibitory effect of transfected T lymphocytes on C1498 tumor cell growth because each type of pathogenic cell has its distinct anatomic location and mechanism of pathogenesis.

The arguments to rejections under 35 USC 103 are not persuasive. The applicants argue that the emphasize of their arguments against obviousness are essentially "lack of motion to combine". However, such motion or motivation could be seen in each and every reference cited. In Chan references (Blood 1995, 1996), the fusion toxin produced by the plasmid construct encoding mGM-CSF and DT390 was used to targeting DT390 to cells expressing GM-CSF receptor including malignant hematological cells. The Chen (Nature 1997) and Yang (Nat. Biotech 1997), clearly teach a retroviral viral vector encoding an antibody fragment as targeting domain and a toxin domain, which was used to transfect T lymphocytes (Jurkat cells) to create antigen-specific killer cells which have high affinity to HIV-infected cells, or HER2+ tumor cells. Therefore, each of the four references teaches targeting the toxin domain to a pathogenic cell via a targeting domain, whether the targeting domain is an antibody or a cytokine; and Chen (Nature 1997) and Yang (Nat. Biotech 1997) references clear teach transfected T lymphocytes as the vehicle for targeting. The combined teachings of the four references illustrate that the cytokine-receptor directed targeting of various toxin via transfected T lymphocytes are well known generally in the art. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by Chan et al, Chen et al and Yang et al, by simply selecting a desired targeting and toxin domain of interest and a vector of interest for transfecting T cells with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention according to the type of the pathogen cells and the specificity, strength and availability of toxic materials. Thus, the claimed invention as a whole was prima facie obvious in the absence of evidence to the contrary. In response to applicant's argument that there is no motivation to combine, it is noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); and the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). .